Opioid as Pharmakon: Harm and Healing from the 19th Century to the Present Day

Mishka Terplan MD MPH
Medical Director
Behavioral Health System Baltimore
Disclosures

• None
The Poppy Goddess
Classical Greece: Foundation of western civilization

- Empire
- Knowledge
- Where we begin our historical narrative

- Regulation of behaviors – individual needs not in conflict with the polis
  - Eros
  - Ekstasis
Dionysus
Demeter
Greek “Wine” and the Golden Mean

• Wine technologies in ancient Greece
• Molecular archaeology
• “Golden Mean” / “Moderation” reflected potency of other substance in wine more than avoidance of alcohol intoxication per se
Pharmakon in the Odyssey

• “Heart’s ease, dissolving anger, magic to make use forget our pains .... No one who drank it deeply, mulled in wine, could let a tear roll down his cheeks that day, not even if right before his eyes some enemy brought down a brother or darling son with a sharp bronze blade. So cunning the drugs that Zeus’s daughter plied.” (Odyssey 4.245-52)
Opioids as Pharmakon

• Ancient Greek term Pharmakon
  – Medicine and Poison
  – The capacity to be beneficial and detrimental – (even at the same time)
  – Third meaning - scapegoat
History

• c3400 BC – poppy cultivated in Lower Mesopotamia “Hul Gil” “joy plant” (Sumerian)
• c1300 BC – Egyptian cultivation – traded into Europe
• c460 Hippocrates
• 1300-1500 disappears from European historical record
• 1527 Paracelsus reintroduces opium as laudanum: black pills opium, citrus and gold – prescribed as painkillers “stones of immortality”
• 1680 Syndeham’s Laudanum introduced – opium, sherry and herbs
• 1803 morphine isolated from poppy
• 1821 De Quincey “Confessions of an English Opium-eater”
• 1843 syringe invented
• 1874 heroin synthesized from morphine marketed in 1890s
19th Century Medicinal Uses

- Analgesia (Civil War)
- Cough Suppressant
- Anti-Diarrhea
- Treatment of “Female Conditions” including (chronic) pain
# Opioid Epidemics in the US

<table>
<thead>
<tr>
<th></th>
<th>1900</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Individuals with opioid use disorder</strong></td>
<td>300,000</td>
<td>2,456,000</td>
</tr>
<tr>
<td><strong>Population of US</strong></td>
<td>76,212,168</td>
<td>321,216,397</td>
</tr>
<tr>
<td><strong>Prevalence of opioid use disorder</strong></td>
<td>0.39%</td>
<td>0.76%</td>
</tr>
</tbody>
</table>
Turn of the century treatment: Addiction is a disease

- Addiction – seen as a medical condition and treated like one
  - Short acting opioids
  - Specialty clinics – detoxification and maintenance

Dr Benjamin Rush
Early 20th Century

- 1914 Harrison Narcotics Tax Act
  - Regulated manufacture and distribution of opioids (and cocaine)
  - Licensing of pharmacists and physicians
- Permitted dispensing opioids “to a patient in the course of [the physician’s] professional practice only”
- 1919 Supreme Court Cases – contesting/clarifying role of opioid prescribing for individuals with addiction
- Rendered illegal the prescribing/dispensening of opioids for “maintenance” of opioid use disorders
- 1919 - 1935 c 25,000 physicians indicted for violation of Harrison Act
- All morphine maintenance clinics closed
- Medical treatment for opioid use disorders – virtually disappears
How the Epidemic of Drug Overdose Deaths Ripples Across America

By HAEYOUN PARK and MATTHEW BLOCH  JAN. 19, 2016

Overdose deaths per 100,000

4  8  12  16  20

2003  2004  2005  2006
2007  2008  2009  2010
2011  2012  2013  2014

MARYLAND
Patient Safety CENTER
How the Epidemic of Drug Overdose Deaths Ripples Across America

By HAEYOUN PARK and MATTHEW BLOCH JAN. 19, 2016

129 Americans die each day from drug overdose. More than half are from prescription drugs alone.
Overdose – leading cause of injury death since 2014
More deaths than handguns or motor vehicle accidents
The Current Opioid Epidemic(s)

Iatrogenic

2012 259,000,000 opioid prescriptions for pain

Enough for every adult in US to have month supply

Overdose death (2004-2010) increased:

237% for men
400% for women
In Victoria County, Tex., a rural area near the Gulf Coast, deaths among women 45 to 54 have climbed by 169 percent in that time period, the sharpest increase in that age group of any U.S. county. The death rate climbed from 216 per 100,000 people to 583.
The Current Opioid Epidemic(s)

Related but distinct epidemics of

– Overprescribing
– Overdose
– Opioid Addiction
  • Heroin, prescription opioids
– NAS – Child Removal
Opioid Over Prescription

Opioid Misuse

Opioid Use Disorder

Opioid Overdose
Not everyone exposed to opioids develops an addiction

Not everyone who dies from an overdose has an addiction
## Women and Prescription Drug Use and Misuse

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prescription</td>
<td>40.9%</td>
<td>47.8%</td>
</tr>
<tr>
<td>psychotherapeutic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>drugs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>“Pain Relievers”</td>
<td>33.9%</td>
<td>38.8%</td>
</tr>
<tr>
<td>Tranquilizers</td>
<td>11.3%</td>
<td>17.9%</td>
</tr>
<tr>
<td>Sedatives</td>
<td>5.6%</td>
<td>8.2%</td>
</tr>
<tr>
<td>Stimulants</td>
<td>6.5%</td>
<td>6.3%</td>
</tr>
</tbody>
</table>

**NSDUH 2015**

*Figure 8. Past Year Misuse of Prescription Psychotherapeutics among People Aged 12 or Older, by Drug Type and Gender: Percentages, 2015*
Initiation of Opioid Misuse

- Past Year Initiates 2015 (NSDUH)
- 2.1 million = 5800 initiates/day
  - 0.9 million males (0.7%)
  - 1.2 million females (0.9%)
Heroin use increasing
Among women especially

## Heroin Use Has INCREASED Among Most Demographic Groups

<table>
<thead>
<tr>
<th>Category</th>
<th>2002-2004*</th>
<th>2011-2013*</th>
<th>% Change</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SEX</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>2.4</td>
<td>3.6</td>
<td>50%</td>
</tr>
<tr>
<td>Female</td>
<td>0.8</td>
<td>1.6</td>
<td>100%</td>
</tr>
<tr>
<td><strong>AGE, YEARS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12-17</td>
<td>1.8</td>
<td>1.6</td>
<td>--</td>
</tr>
<tr>
<td>18-25</td>
<td>3.5</td>
<td>7.3</td>
<td>109%</td>
</tr>
<tr>
<td>26 or older</td>
<td>1.2</td>
<td>1.9</td>
<td>58%</td>
</tr>
<tr>
<td><strong>RACE/ETHNICITY</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic white</td>
<td>1.4</td>
<td>3</td>
<td>114%</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
<td>1.7</td>
<td>--</td>
</tr>
<tr>
<td><strong>ANNUAL HOUSEHOLD INCOME</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than $20,000</td>
<td>3.4</td>
<td>5.5</td>
<td>62%</td>
</tr>
<tr>
<td>$20,000–$49,999</td>
<td>1.3</td>
<td>2.3</td>
<td>77%</td>
</tr>
<tr>
<td>$50,000 or more</td>
<td>1</td>
<td>1.6</td>
<td>60%</td>
</tr>
<tr>
<td><strong>HEALTH INSURANCE COVERAGE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>4.2</td>
<td>6.7</td>
<td>60%</td>
</tr>
<tr>
<td>Medicaid</td>
<td>4.3</td>
<td>4.7</td>
<td>--</td>
</tr>
<tr>
<td>Private or other</td>
<td>0.8</td>
<td>1.3</td>
<td>63%</td>
</tr>
</tbody>
</table>


## Heroin Addiction and Overdose Deaths are Climbing

- **Heroin-Related Overdose Deaths** (per 100,000 people): 286% increase
- **Heroin Addiction** (per 1,000 people)

Opioids are common and proximate
Opioids as Pharmakon

• Ancient Greek term Pharmakon
  – Medicine and Poison
  – The capacity to be beneficial and detrimental – (even at the same time)
How did we get here?
The Current Opioid Epidemic: How did we get here?

More deaths from opioids than homicide in Maryland
Rising morbidity and mortality in midlife among white non-Hispanic Americans in the 21st century

Anne Case¹ and Angus Deaton¹

15078–15083 | PNAS | December 8, 2015 | vol. 112 | no. 49

Fig. 1. All-cause mortality, ages 45–54 for US White non-Hispanics (USW), US Hispanics (USH), and six comparison countries: France (FRA), Germany (GER), the United Kingdom (UK), Canada (CAN), Australia (AUS), and Sweden (SWE).

Fig. 2. Mortality by cause, white non-Hispanics ages 45–54.
Pain: The 5th Vital Sign

• History
  – Introduced by president of American Pain Society 1995
  – Embraced by VA system late 1990s
  – Became Joint Commission standard 2001
    • Bill of Rights for People with Pain

• Because
  – Recognition pain undertreated
  – Untreated pain leads to chronic pain
  – Chronic pain interferes with quality of life, is costly, and common
Joint Commission JCAHO

- Recognize the right of patients, residents or clients to appropriate assessment and management of pain
- Screen patients, residents or clients for pain during their initial assessment and, when clinically required, during ongoing, periodic reassessments
- Educate patients, residents or clients suffering from pain, and their families, about pain management
Screening: The Pain Scale
Treatment of Pain: Opioids

WHO Cancer Pain Ladder

Applied to non-cancer pain

- Opioid addiction rare in pain patients
- Opioids are safe and effective for chronic pain
- Opioid therapy can easily be discontinued
- Physicians needlessly allowing patient to suffer because of “opiophobia”
Education: OxyContin

- Approved 1995; Sales:
  - 1996 $45 million
  - 2000 $1.1 billion
  - 2010 $3.1 billion (30% of painkiller market)

- 1996-2002 Purdue Pharma funded >20,000 pain-related educational programs

- Provided financial support to: American Pain Society, the American Academy of Pain Medicine, the Federation of State Medical Boards, the Joint Commission

- 2007 – Settlement: plead guilty to “criminal charges that they misled regulators, doctors and patients about the drug’s risk of addiction and its potential to be abused” $600M

- Sackler Family (Purdue Pharma) 16th richest in US (Forbes 2015)
Perceptions of Harm

Maryland - Adults

![Pie chart showing perceptions of harm.

Monitoring the Future

Perceptions of Risk – 8th Graders 2013

“How much do you think people risk harming themselves (physically or in other ways), if they...”

<table>
<thead>
<tr>
<th>Activity</th>
<th>Perception</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occasional use of heroin without a needle</td>
<td>73%</td>
</tr>
<tr>
<td>Occasional Vicodin</td>
<td>26%</td>
</tr>
<tr>
<td>Occasional OxyContin</td>
<td>33%</td>
</tr>
<tr>
<td>Occasional Marijuana</td>
<td>37%</td>
</tr>
<tr>
<td>Smoke 1-5 cigarettes/day</td>
<td>43%</td>
</tr>
</tbody>
</table>

Washington Post Survey November 2015
Chronic pain, opioids and addiction: Where’s the Evidence?
ADDICTION RARE IN PATIENTS TREATED WITH NARCOTICS

To the Editor: Recently, we examined our current files to determine the incidence of narcotic addiction in 39,946 hospitalized medical patients who were monitored consecutively. Although there were 11,882 patients who received at least one narcotic preparation, there were only four cases of reasonably well documented addiction in patients who had no history of addiction. The addiction was considered major in only one instance. The drugs implicated were meperidine in two patients, Percodan in one, and hydromorphone in one. We conclude that despite widespread use of narcotic drugs in hospitals, the development of addiction is rare in medical patients with no history of addiction.

JANE PORTER
HERSHEL JICK, M.D.
Boston Collaborative Drug Surveillance Program
Waltham, MA 02154
Boston University Medical Center

Chronic pain, opioids and functional improvement: Where’s the Evidence?
Chronic Use of Opioid Analgesics in Non-Malignant Pain: Report of 38 Cases

Russell K. Portenoy and Kathleen M. Foley
Pain Service, Department of Neurology, Memorial Sloan-Kettering Cancer Center, and Department of Neurology, Cornell University Medical College, New York, NY 10021 (U.S.A.)
(Received 10 June 1985, accepted 28 October 1985)

Summary

Thirty-eight patients maintained on opioid analgesics for non-malignant pain were retrospectively evaluated to determine the indications, course, safety and efficacy of this therapy. Oxycodeone was used by 12 patients, methadone by 7, and levorphanol by 5; others were treated with propoxyphene, meperidine, codeine, pentazocine, or some combination of these drugs. Nineteen patients were treated for four or more years at the time of evaluation, while 6 were maintained for more than 7 years. Two-thirds required less than 20 morphine equivalent mg/day and only 4 took more than 40 mg/day. Patients occasionally required escalation of dose and/or hospitalization for exacerbation of pain; doses usually returned to a stable baseline afterward. Twenty-four patients described partial but acceptable or fully adequate relief of pain, while 14 reported inadequate relief. No patient underwent a

- 11 (29%) adequate pain relief
- 13 (34%) partial relief
- No improvements in social function, employment
- Conclusion: “Opioid maintenance therapy initiated for the treatment of chronic non-malignant pain can be safely and often effectively continued for long periods of time”
Poor Science Widely Cited

Weak evidence regarding COT efficacy and safety was widely cited

![Graph showing cumulative number of citations over years for two studies: Porter and Jick 1980 and Portenoy and Foley 1986.](image)
What’s the evidence today?

- 50% opioid-naïve patients on opioids report no change or worsening pain
- Compared to placebo:
  - Moderate pain relief for opioids – all short term (<12wks) outcomes
  - Increase in short-term adverse events
- No benefit of extended release vs other formulations
- High-dose vs low-dose: no difference in toxicities
Death Rates Rising for Whites

DEATH RATES FOR BLACK AND HISPANIC adults have fallen since 1999, but have increased for WHITES, particularly women and young adults. The rise in deaths has been largely driven by drug overdoses.

DEATHS FROM H.I.V. AND AIDS have fallen steadily among younger blacks and Hispanics, accounting for much of their overall drop in death rates. AIDS-related deaths have also fallen among whites, but not enough to offset the increasing numbers of deaths from suicide and drug overdose.

DEATHS FROM DRUG OVERDOSE and other accidental poisonings have remained relatively flat for blacks and Hispanics but continue to rise sharply among whites. Prescription painkillers and heroin are thought to be driving the increase in drug deaths.

Source: Centers for Disease Control and Prevention
By The New York Times
Trends in Opioid Prescribing by Race/Ethnicity for Patients Seeking Care in US Emergency Departments

Mark J. Pletcher, MD, MPH
Stefan G. Kertesz, MD, MSc
Michael A. Kohn, MD, MPP
Ralph Gonzales, MD, MSPH

Context: National quality improvement initiatives implemented in the late 1990s were followed by substantial increases in opioid prescribing in the United States, but it is unknown whether opioid prescribing for treatment of pain in the emergency department has increased and whether differences in opioid prescribing by race/ethnicity have decreased.

Objectives: To determine whether opioid prescribing in emergency departments has...
Racial Disparities in Pain Management of Children With Appendicitis in Emergency Departments

Monika K. Goyal, MD, MSCE; Nathan Kuppermann, MD, MPH; Sean D. Cleary, PhD, MPH; Stephen J. Teach, MD, MPH; James M. Chamberlain, MD

Figure 1. Predicted Probabilities for Analgesic and Opioid Administration by Race Stratified by Pain Score and Adjusted for Ethnicity

A Moderate pain

B Severe pain

* Statistically significant difference in administration (P < .05).

Figure 2. Adjusted Predicted Probabilities for Analgesia and Opioid Administration by Race Over Time

A Any analgesia

B Opioid analgesia

A, Any analgesia. B, Opioid analgesia. Adjusted for ethnicity, age, sex, insurance status, triage level, and pain score.
Racial bias in pain assessment and treatment recommendations, and false beliefs about biological differences between blacks and whites

Kelly M. Hoffman, Sophie Trawalter, Jordan R. Axt, and M. Norman Oliver

Department of Psychology, University of Virginia, Charlottesville, VA 22904; Department of Family Medicine, University of Virginia, Charlottesville, VA 22908; and Department of Public Health Sciences, University of Virginia, Charlottesville, VA 22908

Edited by Susan T. Fiske, Princeton University, Princeton, NJ, and approved March 1, 2015 (received for review August 18, 2015)

Black Americans are systematically undertreated for pain relative to white Americans. We examine whether this racial bias is related to false beliefs about biological differences between blacks and whites (e.g., “black people’s skin is thicker than white people’s skin”). Study 1 documented these beliefs among white laypersons and revealed that participants who more strongly endorsed false beliefs about biological differences reported lower pain ratings for a black (vs. white) target. Study 2 extended these findings to the medical context and found that half of a sample of white medical students and residents endorsed these beliefs. Moreover, participants who endorsed these beliefs rated the black (vs. white) patient’s pain as lower and made less accurate treatment recommendations. Participants who did not endorse these beliefs rated the black (vs. white) patient’s pain as higher, but showed no bias in treatment recommendations. These findings suggest that individuals with at least some medical training hold and may use false beliefs about biological differences between blacks and whites to inform medical judgments, which may contribute to racial disparities in pain assessment and treatment.

These disparities in pain treatment could reflect an overprescription of medications for white patients, underprescription of medications for black patients, or, more likely, both. Indeed, there is evidence that overprescription is an issue, but there is also clear evidence that the underprescription of pain medications for black patients is a real, documented phenomenon (1, 4). For example, a study examining pain management among patients with metastatic or recurrent cancer found that only 35% of racial minority patients received the appropriate prescriptions— as established by the World Health Organization guidelines—compared with 50% of nonminority patients (4).

Broadly speaking, there are two potential ways by which racial disparities in pain management could arise. The first possibility is that physicians recognize black patients’ pain, but do not treat it, perhaps due to concerns about noncompliance or access to health care (7, 8). The second possibility is that physicians do not recognize black patients’ pain in the first place, and thus cannot treat it. In fact, recent work suggests that racial bias in pain treatment may stem, in part, from racial bias in perceptions of others’ pain. This research has shown that people assume a priori that blacks feel less pain than do whites (11–17). In a study by Staton et al. (14), for instance, patients were asked to report how much pain they were experiencing, and physicians were asked to rate how much pain they thought the patients were experiencing. Physicians were more likely to underestimate the pain of black patients than white patients (11–17).
Study 1: False Beliefs about racial differences

- Blacks age more slowly than whites
- Blacks’ nerve endings are less sensitive than whites’
- Whites have larger brains than blacks
- Blacks’ skin is thicker than whites’
- Black couples are significantly more fertile than white couples
Study 2: Medical Context

- Half of white medical students/residents endorsed false beliefs.
- Those who endorsed false beliefs rated black (vs. white) patient’s pain as lower and made less accurate treatment recommendations.
Racism has “protected” non-whites from the overdose epidemic

- Racial inequities in opioid prescribing exist
- Non-whites less likely to get opioids for pain
- Radically altered death rates for whites
In Heroin Crisis, White Families Seek Gentler War on Drugs

By KATHARINE Q. SEELYE  OCT. 30, 2015

Governors Unite in the War Against Opioids

Senate candidate Rubens says war on drugs has been 'abject failure,' new approach needed

Republican calls for allowing states to use proceeds of legalized marijuana for drug treatment

Bronx Needle Exchange, Once Dismissed, Finds Acceptance

Side Street
By DAVID GONZALEZ  APRIL 17, 2016
Race and the Public and Legal Response to Addiction
The War on Drugs
"The Nixon campaign in 1968, and the Nixon White House after that, had two enemies: the antiwar left and black people. You understand what I'm saying? ... By getting the public to associate the hippies with marijuana and blacks with heroin. And then criminalizing both heavily, we could disrupt those communities ... We could arrest their leaders, raid their homes, break up their meetings, and vilify them night after night on the evening news. Did we know we were lying about the drugs? Of course we did."

- Former Nixon domestic policy chief John Ehrlichman
Every 25 Seconds
The human toll of criminalizing drug use in the US
MD has highest rate of “aggressive policing” in the US

Nationwide, rates of arrest for drug possession range from 700 per 100,000 people in Maryland to 77 per 100,000 in Vermont.
Figure 7: Race disparities in US drug possession arrests
Ratios of arrest rates per race disaggregated 100,000 adult population by state (2014)
Red line indicates equal Black and white arrest rates
Scapegoat is English translation of the Hebrew word Azazel – the goat that departs

A scapegoat is a person or animal which takes on the sins of others, or is unfairly blamed for problems. The concept originally comes from Leviticus, in which a goat is designated to be cast into the desert with the sins of the community. Other ancient societies had similar practices. In psychology and sociology, the practice of selecting someone as a scapegoat has led to the concept of scapegoating.

And Aaron shall place lots upon the two goats: one lot "For the Lord," and the other lot, "For Azazel (for absolute removal)."

— Leviticus 16:8
Opioids and Scapegoat

• The War on Drugs
• We have used drugs to scapegoat people, policies, communities in destructive ways
• Right now the narrative is one of compassion (sort of) but it wouldn’t take much to slip back into villification
The Future

• The opioid epidemic will wane – but addiction in society in general, among pregnant women in particular, won’t go away
• There will be another drug epidemic
• We need to make sure that we use this moment to
  – Truly treat addiction as a disease - decriminalize drug use
  – Make sure that systems are in place assess and treat individuals and their families with the highest quality of care and with compassion and dignity
Thank You

- Mishka Terplan
- Mishka.terplan@bhsbaltimore.org